

We claim:

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1. A method of diagnosing a disorder characterized by expression of a human cancer associated antigen precursor coded for by a nucleic acid molecule, comprising:

contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule is a NA Group 1 nucleic acid molecule, and

determining the interaction between the agent and the nucleic acid molecule or the expression product as a determination of the disorder.

2. The method of claim 1, wherein the agent is selected from the group consisting of

(a)

a nucleotide acid molecule comprising NA group 1 nucleic acid molecules

or a fragment thereof,

(b)

a nucleic acid molecule comprising NA group 3 nucleic acid molecules or

a fragment thereof,

(c)

a nucleic acid molecule comprising NA group 17 nucleic acid molecules

or a fragment thereof,

(d)

an antibody that binds to an expression product of NA group 1 nucleic

acids,

(e)

an antibody that binds to an expression product of NA group 3 nucleic

acids,

(f)  
an antibody that binds to an expression product of NA group 17 nucleic acids,

(g)  
and agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 1 nucleic acid,

(h)  
an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 3 nucleic acid, and

(I)  
an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 17 nucleic acid.

3. The method of claim 1, wherein the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 4, at least 6, at least 7, or at least 8, at least 9 or at least 10 such agents.

4. The method of claims 1-3, wherein the agent is specific for a human cancer associated antigen precursor that is a breast, a gastric, a lung, a prostate, a renal or a colon cancer associated antigen precursor.

5. A method for determining regression, progression or onset of a condition characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising

monitoring a sample, from a patient who has or is suspected of having the condition, for a parameter selected from the group consisting of

(I)

the protein,

(ii)

a peptide derived from the protein,

(iii)

an antibody which selectively binds the protein or peptide, and

(iv)

cytolytic T cells specific for a complex of the peptide derived from the

protein and an MHC molecule,

as a determination of regression, progression or onset of said condition.

6.

The method of claim 5, wherein the sample is a body fluid, a body effusion or a tissue.

7.

The method of claim 5, wherein the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of

(a)

an antibody which selectively binds the protein of (I), or the peptide of (ii),

(b)

a protein or peptide which binds the antibody of (iii), and

(c)

a cell which presents the complex of the peptide and MHC molecule of

(iv).

8. The method of claim 7, wherein the antibody, the protein, the peptide or the cell is labeled with a radioactive label or an enzyme.

9. The method of claim 5, comprising assaying the sample for the peptide.

10. The method of claim 5, wherein the nucleic acid molecule is a NA Group 3 molecule.

11. The method of claim 5, wherein the nucleic acid molecule is a NA Group 11 molecule.

12. The method of claim 5, wherein the nucleic acid molecule is a NA Group 12 molecule.

13. The method of claim 5, wherein the nucleic acid molecule is a NA Group 13 molecule.

14. The method of claim 5, wherein the nucleic acid molecule is a NA Group 14 molecule.

15. The method of claim 5, wherein the nucleic acid molecule is a NA Group 15 molecule.

16. The method of claim 5, wherein the nucleic acid molecule is a NA Group 16 molecule.

17. The method of claim 5, wherein the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins.

5 18. A pharmaceutical preparation for a human subject comprising  
an agent which when administered to the subject enriches selectively the  
presence of complexes of an HLA molecule and a human cancer associated antigen, and  
a pharmaceutically acceptable carrier, wherein the human cancer  
associated antigen is a fragment of a human cancer associated antigen precursor encoded by a  
10 nucleic acid molecule comprises a NA Group 1 molecule.

19. The pharmaceutical preparation of claim 18, wherein the agent comprises  
a plurality of agents, each of which enriches selectively in the subject complexes of an HLA  
molecule and a different human cancer associated antigen.

15 20. The pharmaceutical preparation of claim 19, wherein the plurality is at  
least two, at least three, at least four or at least 5 different such agents.

21. The pharmaceutical preparation of claim 18, wherein the nucleic acid  
20 molecule is a NA Group 3 nucleic acid molecule.

22. The pharmaceutical preparation of claim 18, wherein the agent is selected  
from the group consisting of  
(1) an isolated polypeptide comprising the human cancer associated  
25 antigen, or a functional variant thereof,  
(2) an isolated nucleic acid operably linked to a promoter for expressing  
the isolated polypeptide, or functional variant thereof,  
(3) a host cell expressing the isolated polypeptide, or functional variant  
thereof, and

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~~(4) isolated complexes of the polypeptide, or functional variant thereof,  
and an HLA molecule.~~

23. The pharmaceutical preparation of claims 18-22, further comprising an  
5 adjuvant.

24. The pharmaceutical preparation of claim 18, wherein the agent is a cell  
expressing an isolated polypeptide comprising the human cancer associated antigen or a  
functional variant thereof, and wherein the cell is nonproliferative.

25. The pharmaceutical preparation of claim 18, wherein the agent is a cell  
expressing an isolated polypeptide comprising the human cancer associated antigen or a  
functional variant thereof, and wherein the cell expresses an HLA molecule that binds the  
polypeptide.

26. The pharmaceutical preparation of claim 18, wherein the agent is at least  
two, at least three, at least four or at least five different polypeptides, each coding for a different  
human cancer associated antigen or functional variant thereof.

27. The pharmaceutical preparation of claim 18, wherein the agent is a PP  
Group 2 polypeptide.

28. The pharmaceutical preparation of claim 18, wherein the agent is a PP  
Group 3 polypeptide or a PP Group 4 polypeptide.

29. The pharmaceutical preparation of claim 25, wherein the cell expresses  
one or both of the polypeptide and HLA molecule recombinantly.

30. The pharmaceutical preparation of claim 25, wherein the cell is  
30 nonproliferative.

31 ~~A composition comprising~~  
~~an isolated agent that binds selectively a PP Group 1 polypeptide.~~

32. ~~The composition of matter of claim 31, wherein the agent binds selectively a PP Group 3 polypeptide.~~

33. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 11 polypeptide.

34. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 12 polypeptide.

35. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 13 polypeptide.

36. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 14 polypeptide.

37. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 15 polypeptide.

38. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 16 polypeptide.

39. The composition of claims 31-38, wherein the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides.

~~The composition of claims 31-38, wherein the agent is an antibody.~~



41. The composition of claim ~~39~~, wherein the agent is an antibody.

*Supp*  
42. ~~A composition of matter comprising~~  
~~a conjugate of the agent of claims 31-41 and a therapeutic or diagnostic~~  
~~agent.~~

43. The composition of matter of claim 42, wherein the conjugate is of the agent and a therapeutic or diagnostic that is a toxin.

10 44. A pharmaceutical composition comprising an isolated nucleic acid molecule selected from the group consisting of:

(1)

NA Group 1 molecules, and

15 (2)

NA Group 2 molecules, and a pharmaceutically acceptable carrier.

45. The pharmaceutical composition of claim 44, wherein the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule.

20 46. The pharmaceutical composition of claim 44, wherein the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different human cancer associated antigen.

25 47. The pharmaceutical composition of claims 44-46 further comprising an expression vector with a promoter operably linked to the isolated nucleic acid molecule.

48. The pharmaceutical composition of claims 44-46 further comprising a host cell recombinantly expressing the isolated nucleic acid molecule.

49. ~~A pharmaceutical composition comprising  
an isolated polypeptide comprising a PP Group 1 or a PP Group 2  
polypeptide, and  
a pharmaceutically acceptable carrier.~~

50. The pharmaceutical composition of claim 49, wherein the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.

51. The pharmaceutical composition of claim 49, wherein the isolated polypeptide comprises at least two different polypeptides, each comprising a different human cancer associated antigen.

52. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 11 polypeptides or HLA binding fragments thereof.

53. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 12 polypeptides or HLA binding fragments thereof.

54. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 13 polypeptides or HLA binding fragments thereof.

55. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 14 polypeptides or HLA binding fragments thereof.

56. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 15 polypeptides or HLA binding fragments thereof.

57. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 16 polypeptides or HLA binding fragments thereof.

~~58. The pharmaceutical composition of claims 49-57, further comprising an adjuvant.~~

59. An isolated nucleic acid molecule comprising a NA Group 3 molecule.

60. An isolated nucleic acid molecule comprising a NA Group 4 molecule.

61. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 11 molecule or a fragment thereof.

62. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 12 molecule or a fragment thereof.

63. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 13 molecule or a fragment thereof.

64. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 14 molecule or a fragment thereof.

65. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 15 molecule or a fragment thereof.

66. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 16 molecule or a fragment thereof.

67. An isolated nucleic acid molecule selected from the group consisting of

(a)

a fragment of a nucleic acid selected from the group of nucleic acid  
consisting of SEQ ID NOs presenting nucleic acid sequences among SEQ ID NOs. 1-816, of  
5 sufficient length to represent a sequence unique within the human genome, and identifying a  
nucleic acid encoding a human cancer associated antigen precursor,

(b)

complements of (a),

10 provided that the fragment includes a sequence of contiguous nucleotides  
which is not identical to any sequence selected from the sequence group consisting of

(1) sequences having the GenBank accession numbers of Table 1

(correct?),

15 (2) complements of (1), and

(3) fragments of (1) and (2).

68. The isolated nucleic acid molecule of claim 67, wherein the sequence of  
contiguous nucleotides is selected from the group consisting of:

20 (1)

at least two contiguous nucleotides nonidentical to the sequence group,

(2)

at least three contiguous nucleotides nonidentical to the sequence group,

(3)

25 at least four contiguous nucleotides nonidentical to the sequence group,

(4)

at least five contiguous nucleotides nonidentical to the sequence group,

(5)

30 at least six contiguous nucleotides nonidentical to the sequence group,

(6)  
at least seven contiguous nucleotides nonidentical to the sequence group.

69. The isolated nucleic acid molecule of claim 67, wherein the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

70. The isolated nucleic acid molecule of claim 67, wherein the molecule encodes a polypeptide which, or a fragment of which, binds a human HLA receptor or a human antibody.

71. An expression vector comprising an isolated nucleic acid molecule of claims 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69 or 70 operably linked to a promoter.

72. An expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule.

73. An expression vector comprising a NA Group 1 or Group 2 molecule and a nucleic acid encoding an HLA molecule.

74. A host cell transformed or transfected with an expression vector of claims 71, 72, or 73.

75. A host cell transformed or transfected with an expression vector of claim 71 or claim 72 and further comprising a nucleic acid encoding HLA.

76. An isolated polypeptide encoded by the isolated nucleic acid molecule of claims 59, 60, 61, 62, 63, 64, 65, or 66.

77. ~~A fragment of the polypeptide of claim 76 which is immunogenic.~~

78. The fragment of claim 77, wherein the fragment, or a portion of the fragment, binds HLA or a human antibody,

5

~~79. An isolated fragment of a human cancer associated antigen precursor which, or portion of which, binds HLA or a human antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule.~~

10 80. The fragment of claim 79, wherein the fragment is part of a complex with HLA.

81. The fragment of claim 79, wherein the fragment is between 8 and 12 amino acids in length.

15

~~82. An isolated polypeptide comprising a fragment of the polypeptide of claim 76 of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that is a human cancer associated antigen precursor.~~

20 83. A kit for detecting the presence of the expression of a human cancer associated antigen precursor comprising  
a pair of isolated nucleic acid molecules each of which consists essentially  
of a molecule selected from the group consisting of

25 (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of  
any of the NA Group 1 molecules and

(b) complements of ("a"), wherein the contiguous segments are  
nonoverlapping.

30

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84. The kit of claim 83, wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule.

5 85. A method for treating a subject with a disorder characterized by expression of a human cancer associated antigen precursor, comprising administering to the subject an amount of an agent, which enriches selectively in the subject the presence of complexes of an HLA molecule and a human cancer associated antigen, effective to ameliorate the disorder, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of

(a)  
a nucleic acid molecule comprising NA group 1 nucleic acid molecules,

(b)  
a nucleic acid molecule comprising NA group 3 nucleic acid molecules,

(c)  
a nucleic acid molecule comprising NA group 17 nucleic acid molecules.

86. The method of claim 85, wherein the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human cancer associated antigen.

87. The method of claim 86, wherein the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

88. The method of claims 85-87, wherein the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4, PP Group 5, PP Group 6, PP Group 7, PP Group 8, PP Group 9, PP Group 10, PP Group 11, PP Group 12, PP Group 13, PP Group 14, PP Group 15, PP Group 16 and PP Group 17 polypeptides.

89. The method of claims 85-88, wherein the disorder is cancer.

90. A method for treating a subject having a condition characterized by expression of a human cancer associated antigen precursor in cells of the subject, comprising:

(I) removing an immunoreactive cell containing sample from the subject,

(ii) contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human cancer associated antigen which is a fragment of the precursor,

(iii) introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer-associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from the group of nucleic acid molecules consisting of NA Group 1, NA Group 2, NA Group 3, NA Group 4, NA Group 5, NA Group 6, NA Group 7, NA Group 8, NA Group 9, NA Group 10, NA Group 11, NA Group 12, NA Group 13, NA Group 14, NA Group 15, NA Group 16, and NA Group 17.



91. The method of claim 90, wherein the host cell recombinantly expresses an HLA molecule which binds the human cancer associated antigen.

92. The method of claim 90, wherein the host cell endogenously expresses an HLA molecule which binds the human cancer associated antigen.

93. A method for treating a subject having a condition characterized by expression of a human cancer associated antigen precursor in cells of the subject, comprising:

(I)  
identifying a nucleic acid molecule expressed by the cells associated with said condition, wherein said nucleic acid molecule is a NA Group 1 molecule

(ii)  
transfecting a host cell with a nucleic acid selected from the group consisting of

(a) the nucleic acid molecule identified,  
(b)  
a fragment of the nucleic acid identified which includes a segment coding for a human cancer associated antigen,

(c)  
deletions, substitutions or additions to (a) or (b), and

(d)

degenerates of (a), (b), or (c);

(iii)

culturing said transfected host cells to express the transfected nucleic acid

molecule, and;

(iv)

introducing an amount of said host cells or an extract thereof to the subject

effective to increase an immune response against the cells of the subject associated with the condition.

94.

The method of claim 93, further comprising:

(a)

identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule,

wherein the host cell expresses the same MHC molecule as identified in (a) and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.

95.

The method of claim 93, wherein the immune response comprises a B-cell response or a T cell response.

96.

The method of claim 95, wherein the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human cancer associated antigen.

97. The method of claim 93, wherein the nucleic acid molecule is a NA Group 3 molecule.

98. The method of claims 93 or 94, further comprising treating the host cells to render them non-proliferative.

99. ~~A method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.~~

100. The method of claim 99, wherein the antibody is a monoclonal antibody.

101. The method of claim 100, wherein the monoclonal antibody is a chimeric antibody or a humanized antibody.

102. A method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject a pharmaceutical composition of any one of claims 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 47, and 58 in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject.

103. The method of claim 102, wherein the condition is cancer.

104. The method of claims 102-103, further comprising first identifying that the subject expresses in a tissue abnormal amounts of the protein.

105. ~~A method for treating a subject having a condition characterized by~~  
expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA  
Group 1 nucleic acid molecule, comprising

(i) identifying cells from the subject which express abnormal amounts of  
the protein;

(ii) ~~isolating a sample of the cells;~~

(iii) ~~cultivating the cells, and~~

(iv) ~~introducing the cells to the subject in an amount effective to provoke~~  
~~an immune response against the cells.~~

106. The method of claim 105, wherein the cells express a protein selected  
from the group  
consisting of a PP Group 11 protein, a PP Group 12 protein, a PP Group 13 protein, PP Group 14  
protein, a PP Group 15 protein and a PP Group 16 protein.

107. The method of claim 105, further comprising rendering the cells non-  
proliferative, prior to introducing them to the subject.

108. ~~A method for treating a pathological cell condition characterized by~~  
aberrant expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic  
acid molecule, comprising  
~~administering to a subject in need thereof an effective amount of an agent~~  
~~which inhibits the expression or activity of the protein.~~

109. The method of claim 108, wherein the agent is an inhibiting antibody  
which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a  
chimeric antibody or a humanized antibody.

110. The method of claim 108, wherein the agent is an antisense nucleic acid  
molecule which selectively binds to the nucleic acid molecule which encodes the protein.

111. The method of claim 108, wherein the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

5 ~~112. A composition of matter useful in stimulating an immune response to a plurality of a protein encoded by nucleic acid molecules that are NA Group 1 molecules, comprising~~  
~~a plurality of peptides derived from the amino acid sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.~~

10 113. The composition of matter of claim 112, wherein at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto.

15 114. The composition of matter of claim 113, further comprising an adjuvant.

115. The composition of matter of claim 114, wherein said adjuvant is a saponin, GM-CSF, or an interleukin.

20 ~~116. An isolated antibody which selectively binds to a complex of:~~

(i)  
a peptide derived from a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule and

25 (ii)  
and an MHC molecule to which binds the peptide to form the complex,  
~~wherein the isolated antibody does not bind to (i) or (ii) alone.~~

30 117. The antibody of claim 116, wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

add p<sup>2</sup>  
add p<sup>3</sup>

add  
C4